## **AMENDMENTS**

## Amendments to the Claims

1-30. (Canceled)

- 31. (Currently amended) A composition comprising <u>an active Clostridial neurotoxin joined to a</u> drug or other bioactive molecule;
  - i) a Clostridial neurotoxin light chain which has enzymatic activity for a target substrate selected from the group consisting of SNAP 25, VAMP and Cellubrevin, and
  - ii) a Clostridial neurotoxin heavy chain which has binding specificity for a target nerve cell; and
  - b) a drug or other bioactive molecule joined to the light chain of the active neurotoxin,

wherein the active neurotoxin <u>has binding specificity for a target nerve cell</u>, is internalizable by the target nerve cell <u>and has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin</u>.

- 32. (Currently amended) The composition of claim 31 wherein the <u>active Clostridial</u> neurotoxin is an active botulinum neurotoxin comprises a light chain selected from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum toxin C, botulinum toxin D, botulinum toxin E, a botulinum toxin F, and botulinum toxin G.
- 33. (Cancelled)
- 34. (Currently amended) The composition of claim 31 claim 32 wherein the active botulinum neurotoxin comprises a heavy chain is selected from the group consisting of: tetanus toxin, a botulinum toxin A, a botulinum toxin B, a botulinum toxin C1, a botulinum toxin D, a botulinum toxin E, a botulinum toxin F, and a botulinum toxin G.

Application No.: 09/676,053 17044CPADIV (BOT)

Dolly et al., Modification of Clostridial Toxins for Use as Transport Proteins

35-36 (Cancelled)

37. (Currently amended) A pharmaceutical composition for treatment of a neuromuscular

dysfunction in a mammal, comprising:

a) an active Clostridial neurotoxin comprising joined to a drug or other bioactive molecule;

<u>and</u>

i) a Clostridial neurotoxin light chain which has enzymatic activity for a target

substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin,

and

ii) a Clostridial neurotoxin heavy chain which has binding specificity for a target nerve

cell; and

b) a drug or other bioactive molecule joined to the light chain of the active neurotoxin, a

pharmaceutically acceptable excipient;

wherein the active neurotoxin has binding specificity for a target nerve cell, is internalizable

by the target nerve cell and has enzymatic activity for a target substrate selected from the

group consisting of SNAP-25, VAMP and Cellubrevin a pharmaceutically acceptable

excipient.

38. (Currently amended) The pharmaceutical composition of claim 37 wherein the active

Clostridial neurotoxin comprises a light chain is an active botulinum neurotoxinselected

from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum

toxin C, botulinum toxin D, botulinum toxin E, botulinum toxin F, and botulinum toxin G.

39. (Currently amended) The pharmaceutical composition of claim 37 wherein the active

botulinum neurotoxin comprises a heavy chain is selected from the group consisting of:

3 of 10

Dolly et al., Modification of Clostridial Toxins for Use as Transport Proteins

tetanus toxin, <u>a</u> botulinum toxin A, <u>a</u> botulinum toxin B, <u>a</u> botulinum toxin C1, <u>a</u> botulinum toxin C, a botulinum toxin E, a botulinum toxin F, and <u>a</u> botulinum toxin G.

- 40. (Previously presented) The pharmaceutical composition of claim 37 wherein the neuromuscular dysfunction is characterized by uncontrollable muscle spasms.
- 41. (Previously presented) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is an inhibitor of neurotransmitter release.
- 42. (Previously presented) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is an active ingredient for treatment of botulism or tetanus.
- 43. (Previously presented) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is selected from the group consisting of a GABA agonist, a neuronal calcium channel agonist, an adenosine agonist, a glutamate antagonist, a protein synthesis toxin, a zinc-dependent protease inhibitor, a neuronal growth factor, an antiviral agent, a nicotinic antagonist, a neuronal calcium channel blocker, an acetylcholine esterase inhibitor, a potassium channel activator, a vasamicol or a vasamicol inhibitor, a ribozyme, and a transcribable gene.
- 44. (New) The composition of claim 31 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin.
- 45. (New) The composition of claim 37 wherein the active Clostridial neurotoxin is an active tetanus neurotoxin.